

Favorable action on the merits is solicited.

Respectfully submitted,

Osamu NISHIMURA et al.

By Warren Cheek  
Warren M. Cheek, Jr.  
Registration No. 33,367  
Attorney for Applicants

WMC/dlk  
Washington, D.C. 20006-1021  
Telephone (202) 721-8200  
Facsimile (202) 721-8250  
May 7, 2001

SPECIFICATION

Method for Removing N-terminal Methionine

This application is a 371 of PCT/JP99/05456 filed October 4, 1999.

FIELD OF THE INVENTION

5        This invention relates to a method for the  
efficient removal, from peptides (including proteins)  
or salts thereof which possess an optionally oxidized  
N-terminal methionine residue or diketone of said  
methionine residue, of the N-terminal methionine  
10   residue or the diketone of said methionine residue, in  
the presence of acetic acid and sodium formate, formic  
acid and sodium formate, or formic acid and sodium  
acetate; and to a method for manufacturing peptides or  
salts thereof which do not possess an optionally  
15   oxidized N-terminal methionine residue or diketone of  
said methionine residue.

BACKGROUND ART

20        When protein is biosynthesized within a cell, its  
N-terminal is known to start with methionine, which  
corresponds to the initiation codon AUG of the mRNA.  
However, as this methionine is removed by subsequent  
processing, it is usually no longer present in the  
completed mature protein molecule.

25        With advancements in recombinant DNA techniques,  
it has become possible to produce useful proteins using  
microorganisms and/or animal cells, for example  
*Escherichia coli*. There have been instances wherein  
protein produced via this type of method was found to  
30   retain a residue comprised of the aforementioned  
methionine. For example, the retention rate of  
methionine was as high as approximately 100% in human  
growth hormone expressed in *E. coli* [Nature, 293, 408  
(1981)], and 50% in interferon- $\alpha$  [J. Interferon Res., 1,  
35   381 (1981)], while in nonglycosylated human  
interleukin-2 the presence of a molecular species with

09806871.050704  
FO/050 T/890880